Ethylene Glycol Monophenyl Ether

CAS #122-99-6
Swiss CD-1 mice, at 0.0, 0.25, 1.25, 2.5% in feed
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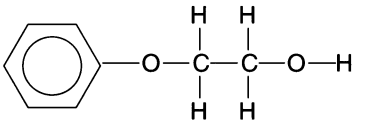

Ethylene glycol monophenyl ether (EGPE), a common chemical and solvent used in industry and in consumer goods, was tested for reproductive toxicity in Swiss CD-1 mice using the RACB protocol (Heindel et al., Fundam Appl Toxicol 15:683–696 [1990]). It was part of a series of glycol ethers and congeners evaluated for structure–activity correlations using this design. Data collected on body weights, clinical signs, and food and water consumption during the dose-range-finding segment (Task 1) were used to set concentrations for the main study (Task 2) at 0.0, 0.25, 1.25, and 2.5% in feed. These concentrations produced calculated consumption estimates of approximately 375, 1875, and 3700 mg/kg/day.

There were no effects on body weight during the continuous breeding phase of the study. Two control mice died, and one mouse and two mice died in the middle- and high dose groups, respectively.

All pairs of mice in each group had at least 1 litter. There was no reduction in the mean number of litters per pair. The middle dose group had 5.00 litters per pair, while the control had a mean of 4.84; this difference was statistically significant, but biologically insignificant. The high dose group had 19% fewer live pups per litter than controls; the live pup weight (adjusted for litter size) was reduced by 4 and 10% in the middle and high dose groups, respectively.

Because of the reduction in pup number, a crossover mating trial was conducted, using one treated partner and one control partner. A separate group of rerandomized controls served as concurrent controls for this task. While there were no alterations in mating or fertility indices or in the number of live pups per litter seen in groups with a treated partner, live pup weight adjusted for litter size was reduced by 12% in the control male × 2.5% EGPE female group. Thus, there was a clear effect in treated females, but one probably related to developmental toxicity rather than female fertility per se.

The control and high dose F_0 mice were killed and necropsied. The treated males weighed 6% less than their controls, while their absolute liver weight was 14% greater. Female body weight was unchanged by EGPE, but absolute liver weight was increased by 55%. No other organ weights were affected. Sperm indices (% motile, epididymal concentration, morphology) were unaffected by EGPE treatment at 2.5%.

The last F_1 litter from all dose levels in Task 2 was reared by the dams to weaning, and then dosed with EGPE at the same concentration provided to their parents. There was reduced body weight gain to weaning: the middle and high dose groups weighed 25 and 58% less than controls at weaning on postnatal day 21; on postnatal day 74, the weight differences were 11 and 17%, respectively. Mortality was also increased in the middle and high dose groups from weaning to mating at postnatal day 74. This was most pronounced in the high-dose group: of the 56 pups weaned in this group, only a total of 6 survived to mating at postnatal day 74. Because this provided too few animals to analyze, this group was omitted from the rest of the study.

At the mating of the second generation, there was no treatment-related effect on F_2 pup number or sex ratio. F_2 pup weight adjusted for litter size was reduced in the 1.25% group by 7%, as was the adjusted liver weight (up 11% in males and 15% in females).

After the delivery of the F_2 pups, the control and 1.25% group F_1 mice were killed and necropsied. The 1.25% EGPE mice weighed 13% less than controls, their absolute testis weight was 16% less, and relative seminal vesicles weight was 14% less than controls. The 1.25% EGPE females weighed 7% less than controls; there were no adjusted weight changes in the treated females. There were no treatment-related alterations in epididymal sperm concentration, motility, or morphology.

In summary, ethylene glycol monophenyl ether produced significant reproductive and developmental toxicity at doses that increased liver weight in treated F_0 and F_1 mice. Ethylene glycol monophenyl ether caused significant toxicity in growing animals, as evidenced by the reduced body weight in neonates in Tasks 2, 3, and 4, and the large increase in postnatal lethality as the F_1 animals grew to the age of mating.

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: **PB85146140/AS**
Chemical: **Ethylene Glycol Monophenyl Ether**
CAS#: **122-99-6**
Mode of exposure: **Feed**
Species/strain: **Swiss CD-1 mice**

F_0 generation — Dose concentration →	0.25%	1.25%	2.5%
General toxicity	Male, female	Male, female	Male, female
Body weight	—, —	—, —	↓, —
Kidney weight[a]	•	•	•
Liver weight[a]	•	•	↑, ↑
Mortality	—	—	—
Feed consumption	—, —	—, —	—, —
Water consumption	•	•	•
Clinical signs	—	—	—
Reproductive toxicity			
x̄ litters/pair	—	↑	—
# live pups/litter; pup wt./litter	—, —	—, ↓	↓, ↓
Cumulative days to litter	—	—	—
Absolute testis, epididymis weight[a]	•	•	—, —
Sex accessory gland weight[a] (prostate, seminal vesicle)	•	•	—, —
Epidid. sperm parameters (#, motility, morphology)	•	•	—, —, —
Estrous cycle length	•	•	•

Determination of affected sex (crossover)	Male	Female	Both
Dose level	•	2.5%	•

F_1 generation — Dose concentration →	0.25%	1.25%	2.5%
General toxicity	Male, female	Male, female	Male, female
Pup growth to weaning	—, —	↓, ↓	↓, ↓
Mortality	•	↑	↑
Adult body weight	—, —	↓, ↓	↓, ↓
Kidney weight[a]	•	•	•
Liver weight[a]	•	↑, ↑	•
Feed consumption	—, —	↑, —	↑, ↑
Water consumption	•	•	•
Clinical signs	•	•	•
Reproductive toxicity			
Fertility index	—	—	—
# live pups/litter; pup wt./litter	—, —	—, ↓	—, —
Absolute testis, epididymis weight[a]	•	↓, —	•
Sex accessory gland weight[a] (prostate, seminal vesicle)	•	—, ↓	•
Epidid. sperm parameters (#, motility, morphology)	•	—, —, —	•
Estrous cycle length	•	•	•

Summary information	
Affected sex?	Female
Study confounders:	None
F_1 more sensitive than F_0?	No
Postnatal toxicity:	Yes

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change ($p<0.05$); —, —, no change in males or females. [a]Adjusted for body weight.